PATENT COOPERATION TREATY PCT/PTO

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	13.09.2004
Applicant's or agent's file reference: 227/03620	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IL 03/00534	25.06.2003	25.06.2002

Applicant: GLUCON INC. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 227/03620	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IL 03/00534	International filing date *(day/month/year)* 25.06.2003	Priority date *(day/month/year)* 25.06.2002
International Patent Classification (IPC) or both national classification and IPC A61B18/00		
Applicant GLUCON INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22.01.2004	13.09.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Abraham, V Telephone No. +49 30 25901-563

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IL 03/00534

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-20 as originally filed

Claims, Numbers

1-40 filed with telefax on 22.08.2004

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-40
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-40
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-40
	No:	Claims	

2. Citations and explanations

   see separate sheet

Reference is made to the following documents:

D1: US-B1-6 200 310 (YARON URI ET AL) 13 March 2001

D2: US-A-5 348 002 (CARO RICHARD G) 20 September 1994

D4: US-A-5 893 848 (NEGUS CHARLES CHRISTOPHER ET AL) 13 April 1999

V

1. Devices for forming a hole in a region of the heart muscle are generally known from the art. Documents D1 and D4 disclose corresponding devices comprising means for removing tissue.

   The subject-matter of claim 1 differs from these documents in that the apparatus further comprises a light source that illuminates the region with non-ablating light that generates photoacoustic waves therein, at one acoustic sensor that generates signals responsive to the photoacoustic waves and a controller that receives the signals and processes them to determine a depth of the hole.

   The problem to be solved by the subject-matter of claim 1 is to provide an alternate depth control.

   In documents D1 and D4 the depth profiling may also be performed acoustically but the acoustic signal is a conventional ultrasonic signal created a acoustic transducer (D1: fig. 4; D4: fig. 11). Although photoacoustical spectroscopy using a light source is known for determination of analyte concentration inside the tissue (see for example document D4: column 6, lines 18-30) it would not be obvious to replace the ultrasonic with a photoacoustic depth profiling. The subject-matter of claim 1 does therefore involve an inventive step and the requirements of Article 33(2)-(4) PCT are met.

2. Claims 2-40 are dependent on claim 1 and therefore also meet the requirements of Article 33(2)-(4).

3. The independent claim should have been drafted in the two part form in accordance with Rule 6.3(b) PCT, with those features known in combination from the prior art being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in a characterising part (Rule 6.3(b)(ii) PCT).

4. The features of the claims should have been provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

5. According to Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D4 should have been mentioned in the description.

10/519023
DT01 Rec'd PCT/PT 22 DEC 2004

CLAIMS

1. Apparatus for forming a hole in a region of the heart muscle wall of a patient undergoing myocardial revascularization comprising:

means for removing tissue from the region to form the hole;

a light source that illuminates the region with non-ablating light that generates photoacoustic waves therein;

at least one acoustic sensor that generates signals responsive to the photoacoustic waves; and

a controller that receives the signals and processes them to determine a depth for the hole.

2. Apparatus according to claim 1 wherein the light source illuminates the region with at least one pulse of light at a wavelength at which light is absorbed by a substance in the region whose concentration can be used to assess a degree of ischemia in the region and wherein the controller processes the signals provided by the at least one acoustic sensor to assay the substance.

3. Apparatus according to claim 2 wherein the substance is hemoglobin.

4. Apparatus according to claim 3 wherein the hemoglobin is oxygenated.

5. Apparatus according to claim 2 or claim 3 wherein the substance is cytochrome aa_3 redox.

6. Apparatus according to any of claims 1-5 wherein the light source illuminates the region with at least one pulse of light at a wavelength at which light is absorbed by water and determines temperature of the region responsive to the signals.

7. Apparatus according to claim 6 and comprising a heat pump that generates a temperature difference between tissue in the region and an ambient temperature of the heart wall and wherein the controller thereafter determines temperature of the tissue as a function of time to assess a degree of ischemia in the region.

8. Apparatus according to any of the preceding claims wherein the light source illuminates the region with at least one light pulse prior to forming the hole and the controller processes the signals to determine a thickness of the heart wall in the region.

9. Apparatus according to claim 1 wherein the controller controls the means for removing tissue from the region responsive to the determined depth and stops formation of the hole by the means for removing tissue when a desired hole depth is reached.

10. Apparatus according to any of the preceding claims wherein the hole is formed in a first surface of the heart wall and deepened towards a second surface of the heart wall and and the controller uses the signals generated by the at least one acoustic sensor to determine a thickness of the heart muscle wall between the bottom of the hole and the second surface.

11. Apparatus according to claim 10 wherein the first surface is an inner surface of the heart wall.

12. Apparatus according to claim 10 wherein the first surface is an outer surface of the heart wall.

13. Apparatus according to any of claims 10-12 wherein the controller controls the means for removing tissue from the region responsive to the determined thickness and stops formation of the hole by the means for removing tissue when a desired thickness is reached.

14. Apparatus according to any of the preceding claims wherein the means for removing tissue comprises a source of ablative energy having an output port from which the ablative energy source provides energy for removing heart tissue by ablation.

15. Apparatus according to claim 14 wherein the source of ablative energy illuminates the region with at least one pulse of ablative energy to form the hole.

16. Apparatus according to claim 15 wherein the at least one ablative pulse generates an acoustic shock wave in the region responsive to which the at least one acoustic sensor generates signals that are transmitted to the controller and wherein the controller processes the signals to determine at least one characteristic of the shock waves.

17. Apparatus according to claim 16 wherein the controller controls at least one characteristic of the at least one ablative pulse responsive to the determined at least one characteristic of the shock wave.

18. Apparatus according to claim 17 wherein at least one characteristic of the at least one ablative pulse is at least one of pulse width, rise time, fall time, peak, and energy and repetition rate of the at least one ablative pulse.

19. Apparatus according to any of claims 16-18 wherein the at least one characteristic of the shock wave is at least one of temporal profile, duration, maximum pressure, minimum pressure, average pressure average intensity and integrated intensity of the acoustic shock wave.

20. Apparatus according to any of claims 15-18 wherein the pulse generates an acoustic shock wave and wherein an acoustic sensor of the at least one acoustic sensor generates signals responsive to reflections of acoustic energy from the shock wave which the controller processes to determine a characteristic of the region.

21. Apparatus according to claim 20 wherein the characteristic comprises a depth of the hole.

22. Apparatus according to claim 20 or claim 21 wherein the characteristic comprises a thickness of the heart muscle wall between the bottom of the hole and a surface of the wall.

23. Apparatus according to any of claims 15-22 wherein the at least one acoustic sensor generates signals responsive to an acoustic shock wave generated by the at least one ablative pulse and the controller processes the signals to determine location of the source of the shock waves.

24. Apparatus according to any of claims 15-23 wherein the at least one ablative pulse comprises a plurality of ablative pulses.

25. Apparatus according to any of claims 14-23 wherein the light source illuminates the region with at least one pulse of light after onset of ablation and the controller uses signals generated by the at least one acoustic sensor responsive to photoacoustic waves to assess damage to tissue in the region of the hole caused by ablation.

26. Apparatus according to claim 25 wherein the wavelength of the at least one light pulse is determined so as to increase a difference in the photoacoustic response of damaged tissue relative to undamaged tissue.

27. Apparatus according to claim 25 or claim 26 wherein the damage comprises thermal damage.

28. Apparatus according to any of claims 25-27 wherein the damage comprises acidosis.

29. Apparatus according to any of claims 25-28 wherein the controller controls at least one characteristic of the ablative pulses responsive to the determined damage.

30. Apparatus according to any of claims 14-29 wherein the controller processes the signals from the at least one acoustic sensor to determine a distance of the ablative energy output port to the bottom of the hole.

31. Apparatus according to any of claims 14-30 wherein the ablative energy comprises electromagnetic energy.

32. Apparatus according to any of claims 14-31 wherein the ablative energy comprises acoustic energy.

33. Apparatus according to any of claims 14-32 wherein the ablative energy comprises optical energy.

34. Apparatus according to any of claims 14-33 and comprising a catheter having a drill end that is positioned in a neighborhood of or in contact with the region in order to form the hole and wherein the optical output aperture, the ablative energy output port and an acoustic

sensor of the at least one acoustic sensor are mounted inside the catheter in a neighborhood of the drill end.

35. Apparatus according to any of claims 14-34 wherein the controller processes signals that it receives from the at least one acoustic sensor to determine a location of the ablative energy output port.

36. Apparatus according to any of claims 1-14 and comprising a catheter having a drill end that is positioned in a neighborhood of or in contact with the region in order to form the hole and wherein the optical output aperture and an acoustic sensor of the at least one acoustic sensor are mounted inside the catheter in a neighborhood of the drill end.

37. Apparatus according to any of claims 34-36 wherein the catheter is configured to perform percutaneous myocardial revascularization.

38. Apparatus according to any of claims 34-36 wherein the catheter is configured to perform transmyocardial revascularization.

39. Apparatus according to any of the preceding claims wherein the at least one acoustic sensor comprises an external acoustic sensor coupled to the patient's skin.

40. Apparatus according to any of claims 1-39 wherein the at least one acoustic sensor comprises an acoustic sensor of an ultrasonic imaging device.